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DOI:

[10.1016/j.ajog.2017.12.235](https://doi.org/10.1016/j.ajog.2017.12.235)

*Document Version*

Peer reviewed version

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*Citation for published version (APA):*

Nzelu, D., Dumitrascu-Biris, D., Nicolaides, K. H., & kametas, N. A. (2018). Chronic hypertension: first-trimester blood pressure control and likelihood of severe hypertension, preeclampsia and small for gestational age. American Journal of Obstetrics and Gynecology. <https://doi.org/10.1016/j.ajog.2017.12.235>

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# Accepted Manuscript

Chronic hypertension: first-trimester blood pressure control and likelihood of severe hypertension, preeclampsia and small for gestational age

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PII: S0002-9378(17)32809-0

DOI: [10.1016/j.ajog.2017.12.235](https://doi.org/10.1016/j.ajog.2017.12.235)

Reference: YMOB 12023

To appear in: *American Journal of Obstetrics and Gynecology*

Received Date: 27 October 2017

Revised Date: 9 December 2017

Accepted Date: 21 December 2017

Please cite this article as: Nzelu D, Dumitrascu-Biris D, Nicolaides KH, kametas NA, Chronic hypertension: first-trimester blood pressure control and likelihood of severe hypertension, preeclampsia and small for gestational age, *American Journal of Obstetrics and Gynecology* (2018), doi: 10.1016/j.ajog.2017.12.235.

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**Chronic hypertension: first-trimester blood pressure control and likelihood of severe hypertension, preeclampsia and small for gestational age**

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**Conflict of interest statement:** The authors report no conflict of interest.

**Sources of funding:** No funding was received for this study.

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**Abstract word count:** 439

**Text word count:** 2537

**Condensation**

The pregnancy outcome of chronic hypertension is influenced by the need and response to anti-hypertensive agents at the time of the first prenatal visit.

**Short version of article title**

Stratification of chronic hypertension in pregnancy.

**ABSTRACT**

**Background:** There is extensive evidence that pre-pregnancy chronic hypertension is associated with high risk of development of severe hypertension and preeclampsia and birth of small for gestational age neonates. However, previous studies have not reported whether anti-hypertensive use, blood pressure control or normalization of blood pressure during early pregnancy influence the rates of these pregnancy complications.

**Objective:** To stratify women with pre-pregnancy chronic hypertension according to the use of antihypertensive medications and level of blood pressure control at the first hospital visit during the first-trimester of pregnancy and examine the rates of severe hypertension, preeclampsia and birth of small for gestational age neonates according to such stratification.

**Study Design:** Prospective study of 586 women with pre-pregnancy chronic hypertension, in the absence of renal or liver disease, booked at a dedicated clinic for the management of hypertension in pregnancy. The patients had singleton pregnancies and were subdivided according to findings in their first visit into group 1 (n=199), with blood pressure <140/90 mmHg without antihypertensive medication, group 2 (n=220), with blood pressure <140/90 mmHg with antihypertensive medication and group 3 (n=167), with systolic blood pressure  $\geq 140$  mmHg and or diastolic blood pressure  $\geq 90$  mmHg despite antihypertensive medication. In the subsequent management of these pregnancies our policy was to maintain the blood pressure at 130-140 / 80-90 mmHg with use of antihypertensive medication; antihypertensive drugs were stopped if the blood pressure was persistently less than 130/80 mmHg. The outcome measures were severe hypertension (systolic blood pressure  $\geq 160$  mmHg and / or diastolic blood pressure  $\geq 110$  mmHg), preterm and term preeclampsia (in addition to hypertension at least one of renal involvement, liver impairment, neurological complications or thrombocytopenia), and birth of small for gestational age neonates (birth weight <5<sup>th</sup> percentile for gestational age). The incidence of these complications was compared in the three strata.

**Results:** The median gestational age at presentation was 10.0 (interquartile range 9.1-11.0) weeks. In groups 2 and 3, compared to group 1, there was a significantly higher

body mass index, incidence of black racial origin and history of preeclampsia in a previous pregnancy. There was a significant increase from group 1 to group 3 in incidence of severe hypertension (10.6%, 22.2% and 52.1%), preterm preeclampsia with onset at <37 weeks of gestation (7.0%, 15.9% and 20.4%), and small for gestational age (13.1%, 17.7% and 21.1%), but not term preeclampsia with onset at  $\geq 37$  weeks of gestation (9.5%, 9.1% and 6.6%).

**Conclusions:** In women with pre-pregnancy chronic hypertension, the rates of development of severe hypertension, preterm preeclampsia and small for gestational age are related to use of antihypertensive medications and level of blood pressure control at the first hospital visit during the first-trimester of pregnancy.

**Key words:** Chronic hypertension, Pregnancy, Preeclampsia, Small for gestational age; Severe hypertension; Antihypertensive drugs; Pregnancy outcome.

## Introduction

Chronic hypertension is found in 1-5% of pregnancies and the frequency increases with age and weight and is higher in Black than in White individuals.<sup>1</sup> In most cases the condition precedes the onset of pregnancy (pre-pregnancy) and in others the hypertension develops in the first 20 weeks of pregnancy.<sup>2, 3</sup> In chronic hypertension there is a high risk for development of severe hypertension or preeclampsia (PE) and delivery of small for gestational age (SGA) neonates.<sup>1, 4-9</sup> Pregnancy is associated with substantial decrease in peripheral resistance, from as early as 5 weeks of gestation, and many women with pre-pregnancy chronic hypertension will therefore have normalization in their blood pressure (BP) even without the need for antihypertensive medications.<sup>10</sup> Consequently, women with pre-pregnancy chronic hypertension fall into three broad categories in relation to their BP control when they present to hospital in the first trimester of pregnancy: those with BP <140/90 mmHg without antihypertensive medication (group 1), those with BP <140/90 mmHg with antihypertensive medication (group 2) and those with persistent hypertension (systolic BP  $\geq$ 140 mmHg and or diastolic BP  $\geq$ 90 mmHg) despite antihypertensive medication (group 3). However, previous studies reporting on the association between chronic hypertension and development of severe hypertension or PE and birth of SGA neonates have not distinguished between these three groups of women and have not reported whether anti-hypertensive use, BP control or normalization of BP during early pregnancy influence the rates of pregnancy complications.<sup>1-7</sup> Furthermore, many of the previous studies include women with secondary hypertension, such as those with renal disease, thereby introducing bias since renal disease is a significant risk factor for the development of PE independent of chronic hypertension.<sup>11, 12</sup>

The objective of this study is to stratify women with pre-pregnancy chronic hypertension according to the use of antihypertensive medications and level of BP control at the first hospital visit during the first-trimester of pregnancy and examine the frequency of severe hypertension, PE and SGA according to such stratification.

## Methods

### Study population

This was an analysis of prospectively collected data in the Antenatal Hypertension Clinic at King's College Hospital, London between January 2011 and January 2016. According to local protocols, pregnant women with pre-pregnancy hypertension are referred to this clinic from the first trimester for the management of their pregnancy. The first visit includes recording of maternal demographic characteristics and obstetric, medical and drug history, measurement of maternal weight and height, recording of BP by validated automated devices and in accordance to the recommendations of the American Heart Association,<sup>13, 14</sup> and assessment of renal and liver function, including measurement of 24 hour urine protein and serum creatinine and aspartate transaminase concentration. The frequency of subsequent visits depends on BP control and at a minimum are carried out at 11-13 and 20-24 weeks' gestation and four weekly thereafter until delivery. These visits include measurement of BP, assessment of renal and liver function, urinalysis for proteinuria and ultrasound examination for fetal anatomy and growth. In the management of patients with chronic hypertension our policy is to maintain the BP at 130-140 / 80-90 mmHg throughout pregnancy with use of antihypertensive medication. Antihypertensive drugs are stopped or their dose is reduced if the BP is below 130/80 mmHg in two consecutive visits.

The inclusion criteria for this study were singleton pregnancies with pre-pregnancy chronic hypertension in the absence of renal or liver disease, presenting to the Antenatal Hypertension Clinic at <14 weeks' gestation and resulting in the live birth or stillbirth of non-malformed babies at  $\geq 24$  weeks' gestation. We excluded pregnancies with fetal aneuploidies or major anomalies diagnosed either prenatally or in the neonatal period, and pregnancies ending in miscarriage. All data were collected by two trained research doctors under the supervision of a senior specialist in Maternal-Fetal Medicine.

The study is part of our routine clinical management and the local Research and Development Committee (King's College Hospital NHS Foundation Trust) and Research Ethics Committee (London-Dulwich, NRES Committee) advised that formal



consideration was not required. Data on pregnancy outcomes were collected from the hospital maternity records and the women's general medical practitioners.

### Outcome measures

Women with pre-pregnancy chronic hypertension were stratified into three groups according to their BP control at the first visit to the Antenatal Hypertension Clinic. In group 1, the BP was  $<140/90$  mmHg without antihypertensive medication, in group 2, the BP was  $<140/90$  mmHg with antihypertensive medication and in group 3, the BP was  $\geq 140/90$  despite antihypertensive medication.

The outcome measures were severe hypertension, PE and birth of SGA neonates. Severe hypertension was defined by the presence of systolic BP  $\geq 160$  mmHg and / or diastolic BP  $\geq 110$  mmHg. Superimposed PE was defined according to the ISSHP-2014 guidelines by having in addition to hypertension at least one of the following: renal involvement (proteinuria  $\geq 300$  mg/24h and/or creatinine  $\geq 90$   $\mu\text{mol/L}$  or  $1$  mg/dL), liver impairment (transaminases  $>70$  IU/L), neurological complications (e.g. eclampsia), thrombocytopenia (platelet count  $<150,000/\mu\text{L}$ ).<sup>2</sup> In addition, PE was subdivided according to gestational age at diagnosis into preterm PE with onset at  $<37$  weeks' gestation and term PE with onset at  $\geq 37$  weeks. Small for gestational age (SGA) was defined as birth weight  $<5^{\text{th}}$  percentile for gestational age.<sup>15</sup> As the ISSHP-2014 guidelines recognise that the inclusion of fetal growth restriction in the definition of PE is controversial, we present the data on prevalence of SGA separately to those of the maternal features of the disease.

### Statistical Analysis

Normality of continuous variables was assessed by the Kolmogorov-Smirnov test. Numerical data were expressed as mean (standard deviation) or as median (interquartile range) for normally and non-normally distributed data, respectively. Differences in maternal and pregnancy characteristics at the first hospital visit and pregnancy outcomes were compared between the three groups of pre-pregnancy chronic hypertension by the ANOVA or Kruskal-Wallis tests (for numerical parametric or non-parametric data) with the Bonferroni correction for post-hoc analysis. The Chi-

square test was performed for categorical variables and the Chi-square for trend when the proportions between groups demonstrated an obvious trend. Multivariate logistic regression analysis was performed in order to assess the independent contribution of the three groups to pregnancy outcomes controlling for maternal demographic characteristics.

Statistical analysis was performed using SPSS (Version 22; SPSS Inc, Chicago, IL).

## Results

### Population characteristics

The study population satisfying the inclusion criteria constituted 586 women with pre-pregnancy chronic hypertension. The median gestational age at presentation was 10.0 (interquartile range 9.1-11.0) weeks. According to BP control at first hospital visit 199 were classified as group 1, 220 as group 2 and 167 as group 3. During the study period another 104 women with pre-pregnancy chronic hypertension attended the unit but these were excluded from the study because 31 presented >14 weeks' gestation, 32 had pre-pregnancy renal or liver disease, 23 had a multiple pregnancy, 7 had major fetal anomalies, 37 suffered a miscarriage and 15 had incomplete data.

Maternal characteristics and results of investigations at the first hospital visit in the three groups are compared in Table 1. Approximately 95% of patients in groups 2 and 3 were taking one antihypertensive drug and about 5% were taking two or more drugs. The most commonly used drugs were labetalol (58.4%), methyldopa (28.9%) and slow-release nifedipine (39.3%). In groups 2 and 3, compared to group 1, there was a significantly higher body mass index, incidence of black racial origin and history of PE in a previous pregnancy; there were no significant differences between groups 2 and 3. There was a significant increase from group 1 to group 3 in systolic and diastolic BP and MAP.

### Pregnancy outcome

Pregnancy outcome measures in the three groups of women with chronic hypertension are compared in Table 2 and Figure 1. During the course of pregnancy, in 24.5% of patients in group 2 and in 6.6% in group 3 the BP remained <140/90 mmHg and the antihypertensive drugs were stopped. In group 1, the BP remained <140/90 mmHg throughout pregnancy without the need for antihypertensive medication in 62.8% of patients. Deterioration in BP necessitating the use of two or more antihypertensive medications occurred in 40.1% of women in group 3, 23.6% in group 2 and 5% in group 1.

In parallel to the use of multiple antihypertensive drugs, there was a significant increase from group 1 to group 3 in incidence of severe hypertension (10.6%, 22.2% and 52.1%), total PE (16.6%, 25.0% and 26.9%), preterm PE (7.0%, 15.9% and 20.4%), and SGA with birth weight <5<sup>th</sup> percentile (13.1%, 17.7% and 21.1%), but not term PE (9.5%, 9.1% and 6.6%).

In the multivariate logistic regression analysis, the risk for severe hypertension, after adjustment for maternal characteristics, was 9-fold higher in group 3 and 2.5-fold higher in group 2 compared to group 1 (Table 3). The risks of PE and SGA in groups 2 and 3 were approximately double those of group 1.

### **Comment**

#### Principal findings of the study

The findings of this study demonstrate that in women with pre-pregnancy chronic hypertension presenting in the first-trimester of pregnancy there is a high incidence of severe hypertension (27%), PE (23%) and SGA with birthweight <5<sup>th</sup> percentile (17%). The study has also shown that the incidence of severe hypertension, preterm PE and SGA is related to the use of antihypertensive medications and level of BP control at presentation in the first trimester of pregnancy; the respective incidences increased from 11%, 7% and 13% in those presenting with BP <140/90 mmHg without the need of taking antihypertensive drugs, to 22%, 16% and 18% in those with BP <140/90 mmHg

after use of antihypertensive drugs, and 52%, 20% and 21% in those with BP  $\geq$ 140/90 mmHg despite use of antihypertensive drugs.

A likely explanation for our findings is that the three subgroups of women with pre-pregnancy chronic hypertension represent three hemodynamic profiles at different stages of the disease. Studies in non-pregnant individuals have demonstrated that in the progression from normal BP to mild and then severe hypertension there is increasing impairment in endothelial function which ultimately results in structural remodelling of small arterial resistance vessels leading to relative thickening of the muscular media, vasoconstriction and decreased capacity for vasodilation.<sup>16-19</sup> In normal pregnancy there is early vasodilatation and decrease in peripheral resistance, followed by compensatory increase in blood volume and cardiac output.<sup>10</sup> We postulate that pre-pregnancy chronic hypertension in group 1 represents the early phase of chronic hypertension with mild impairment in endothelial function and consequent ability to achieve the physiological adaptation to early pregnancy with normalization in BP.<sup>18, 19</sup> However, this group, compared to non-chronic hypertension pregnancies, is still at considerably higher risk for subsequent development of severe hypertension and PE. In group 2 there may be moderate endothelial dysfunction preventing sufficient early vasodilatation to achieve normalization in BP; however, the condition is not so severe as to be non-responsive to antihypertensive drugs. Group 3 may represent severe disease with remodelling of small arteries and decreased capacity for response to antihypertensive drugs; such impairment might also predispose to subsequent development of PE and SGA.<sup>18, 19</sup>

Preeclampsia, particularly preterm-PE, is associated with increased risk of subsequent maternal cardiovascular disease.<sup>20-22</sup> In the context of chronic hypertension the cardiovascular disease precedes the onset of pregnancy and the link with PE may be a similar vascular pathology of atherosclerosis; preterm-PE is characterized by acute atherosclerosis in the spiral arteries in the basal plate of the placenta.<sup>23</sup>

#### Strengths and limitations of the study

The strengths of this study are first, prospective examination of a large population of pregnancies with pre-pregnancy chronic hypertension presenting in the first-trimester,

second, exclusion of women with evidence of renal disease, because this is a risk factor for the development of PE independent of chronic hypertension, third, accurate recording of medical and drug history and use of a standardized protocol for measurement of BP, fourth, a standardized policy for strict control of BP throughout pregnancy, and fifth, stratification of patients according to the use of antihypertensive medications and level of BP control at the first hospital visit and reporting of rates of severe hypertension, PE and SGA according to such stratification.

We were not able to undertake placental examination to substantiate our hypothesis that pre-existing endothelial dysfunction leads to placental dysfunction. Another limitation of the study is the lack of long-term postnatal data regarding the severity of chronic hypertension.

#### Comparison with findings of other studies

The association of chronic hypertension with severe hypertension, PE and SGA has been reported previously but not according to findings in the first-trimester.<sup>1-7</sup>

In a study of 109,932 singleton pregnancies in our population attending for routine pregnancy care at 11-13 weeks' gestation the overall incidence of PE was 2.3%, whereas in the subgroup of women with pre-pregnancy chronic hypertension the incidence was 20.6%; after adjustment for potential confounding variables from maternal characteristics, medical and obstetric history, the incidence of both preterm and term PE in women with chronic hypertension was 5-6 times higher than in women without chronic hypertension.<sup>1</sup>

#### Implications of the findings on clinical practice and future research

Our study has highlighted that in women with pre-pregnancy chronic hypertension there is a high-risk of severe hypertension, PE and SGA despite a policy of aiming to maintain the BP at 130-140 / 80-90 mmHg throughout pregnancy. It is uncertain if the incidence of these complications would have been different if the control of BP was tighter, aiming to maintain the BP at <130/80 mmHg, or less tight, aiming for BP at <160/105 mmHg.

In non-pregnant individuals with hypertension, there is evidence that the target BP should be very low, because the risk of cardiovascular disease increases with increasing systolic BP above 115 mmHg;<sup>24</sup> a large trial demonstrated that intensive treatment aiming to maintain the systolic BP at less than 120 mm Hg, as compared with less than 140 mm Hg, resulted in lower rates of fatal and nonfatal major cardiovascular.<sup>25</sup> In pregnancy, there is reluctance to recommend therapy in mild to moderate disease because reduction in BP or the drugs themselves may have an adverse effect on fetal growth.<sup>26, 27</sup> Consequently, the American College of Obstetricians and Gynecologists (ACOG) recommends that in pregnancies of women with chronic hypertension treatment should be initiated only if the systolic BP is  $\geq 160$  mmHg and the diastolic BP is  $\geq 105$  mmHg.<sup>3, 28</sup> However, in these meta-analyses most patients had gestational hypertension, rather than CH and in most studies therapy was initiated in the late second or early third trimester.<sup>26, 27</sup> A trial in women with mild chronic hypertension at 6-13 weeks' gestation, reported no difference in the risk of PE or SGA between a policy of antihypertensive treatment and one of no treatment.<sup>29</sup> A recent trial of women with chronic hypertension or gestational hypertension and diastolic BP of 90-105 mm Hg at a median gestational age of 24 (range 14-33) weeks, compared a policy of tight control in BP with a target diastolic BP of 85 mm Hg with a policy of less-tight control with target diastolic BP of 100 mm Hg; development of severe hypertension was lower in the tight-control group (28% vs. 41%) but there was no significant difference between the two policies in incidence of PE or SGA.<sup>30</sup>

Alternative strategies in the management of pre-pregnancy chronic hypertension presenting in the first-trimester aimed at reducing the risk of PE and SGA include the prophylactic use of aspirin, pravastatin or metformin. In the ASPRE trial, which reported that aspirin (150 mg/day) from 11-14 to 36 weeks' gestation in pregnancies at high-risk for PE was associated with >60% reduction in the incidence of preterm-PE, the beneficial effect of aspirin did not apply in pregnancies with CH.<sup>31, 32</sup> However, there is some evidence that statins and metformin, which inhibit secretion of the angiogenic factor soluble Fms-like tyrosine kinase-1 (sFLT-1) and decrease markers of endothelial dysfunction and inflammation, may reduce the rate of PE.<sup>33-37</sup> Future trials investigating the potential value of such medications in patients with pre-pregnancy chronic hypertension should stratify the population according to the approach proposed in this study because the effect of the drugs is likely to vary according to the severity of the

underlying disease.

### Conclusions

In women with pre-pregnancy chronic hypertension there is a high risk of severe hypertension, PE and SGA and the incidence of these complications is related to the use of antihypertensive medications and level of BP control at presentation in the first trimester of pregnancy.

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**Figure legend**

**Figure 1.** Pregnancy complications in women with pre-pregnancy chronic hypertension

ACCEPTED MANUSCRIPT

**Table 1:** Maternal characteristics and results of investigations at the booking visit in women with pre-pregnancy chronic hypertension stratified according to blood pressure control at first hospital visit.

Clinical feature	Total population (n=586)	No antihypertensives	Antihypertensives		P value
		Normotensive (Group 1, n=199)	Normotensive (Group 2, n=220)	Hypertensive (Group 3, n=167)	
Antihypertensive medications					
One drug, n (%)	363 (61.9)	-	207 (94.1)	156 (93.4)	0.68
Two or more drugs, n (%)	24 (4.1)	-	13 (5.9)	11 (6.6)	0.68
Gestational age in weeks, median (IQR)	9.0 (10.0-11.0)	10.0 (9.3-11.0)	10.0 (9.1-10.8)	10.0 (9.0-10.9)	0.108
Age in years, median (IQR)	35.0 (31.0-38.0)	34.0 (30.0-37.5)*	35.0 (32.0-38.0)	35.0 (31.0-39.0)	0.005
Body mass index in kg/m <sup>2</sup> , median (IQR)	31.0 (26.0-35.0)	28.0 (25.0-33.1)*	31.1 (26.0-35.0)	32.0 (28.0-37.0)	<0.0001
Weight in kg, median (IQR)	83.3 (69.7-95.9)	79.4 (67.0-91.5)*	84.0 (70.6-95.2)	87.8 (73.5-103.1)	<0.0001
Height in meters, median (IQR)	1.65 (1.6.0-1.68.)	165.0 (160.5-169.0)	165.0 (160.0-168.0)	165.0 (160.0-169.0)	0.58
Family history of PE, n (%)	75 (12.8)	25 (12.6)	26 (11.8)	24 (14.4)	0.75
Multiparous, n (%)	403 (68.8)	112 (56.3)*	174 (79.1)	117 (70.1)	<0.0001
Preeclampsia in previous pregnancy, n (%)	230 (39.2)	51 (25.6)*	107 (48.6)	72 (43.1)	<0.0001
Racial origin					
Black, n (%)	359 (61.3)	99 (49.7)*	148 (67.3)	112 (67.1)	<0.0001
Caucasian, n (%)	176 (30.0)	81 (40.7)*	51 (23.2)	44 (26.3)	<0.0001
South-East Asian, n (%)	23 (3.9)	9 (4.5)	13 (5.9)	1 (0.6)	0.07
Other, n (%)	28 (4.8)	10 (5.0)	8 (3.6)	10 (6.0)	0.70
Systolic BP in mmHg, median (IQR)	130 (120-139)	120 (112-130)	124 (120-130)	145 (140-152) <sup>§</sup>	<0.0001
Diastolic BP in mmHg, median (IQR)	80 (74-86)	76 (70-80)	80 (72-81)	90 (84-97) <sup>§</sup>	<0.0001
Serum creatinine in µmol/L, median (IQR)	50 (45-58)	49 (42-57)	51 (46-58)	52 (45-62)	0.005
Aspartate transaminase in IU/L, median (IQR)	19 (16-22)	19 (16-23)	18 (16-22)	18 (16-21)	0.61
24 hour urine protein >300 mg, n (%)	0(0)	0(0)	0(0)	0(0)	-

IQR = interquartile range. P-value <0.05 represents a statistically significant difference between the three subgroups in the Kruskal-Wallis (numerical data) or chi-square for trend (categorical data). \* Statistically significant difference between group 1 compared to groups 2 and 3, <sup>§</sup> Statistically significant difference between group 3 compared to groups 1 and 2.

**Table 2:** Pregnancy outcome in women with pre-pregnancy chronic hypertension stratified according to blood pressure control at first hospital visit.

Outcome	Total population (n=586)	No antihypertensives	Antihypertensives		P value
		Normotensive (Group 1, n=199)	Normotensive (Group 2, n=220)	Hypertensive (Group 3, n=167)	
Severe hypertension, n (%)	159 (27.1)	21 (10.6)	51 (22.2)	87 (52.1)	<0.0001
Antihypertensive medications at delivery					
No drugs, n (%)	190 (32.4)	125 (62.8)	54 (24.5)	11 (6.6)	< 0.0001
One drug, n (%)	267 (45.5)	64 (32.2)*	114 (51.8)	89 (53.3)	
Two or more drugs, n (%)	129 (22.0)	10 (5.0)	52 (23.6)	67 (40.1)	< 0.0001
Preeclampsia, n (%)					
Total, n (%)	133 (22.7)	33 (16.6)	55 (25.0)	45 (26.9)	0.01
Onset <37 weeks, n (%)	83 (14.2)	14 (7.0)	35 (15.9)	34 (20.4)	0.0002
Onset ≥ 37 weeks, n (%)	50 (8.5)	19 (9.5)	20 (9.1)	11 (6.6)	0.32
Gestation at onset, median (IQR)	35.6 (32.7-38.0)	37.1 (34.2-39.0)	35.7 (33.5-37.9)	34.6 (30.1-38.3)	0.09
Small for gestational age, n (%)	100 (17.1)	26 (13.1)	39 (17.7)	35 (21.1)	0.04
Birth weight percentile, median (IQR)	27.2 (8.3-53.3)	30.7 (11.2-56.9)	28.5 (7.3-52.2)	22.4 (7.6-48.8)	0.07
Gestation at delivery, median (IQR)	38.8 (37.5-39.7)	39.1 (38.0-40.0)*	38.7 (37.5-39.5)	38.7 (37.0-39.5)	0.001

IQR = interquartile range. P-value <0.05 represents a statistically significant difference between the three subgroups in the Kruskal-Wallis (numerical data) or chi-square for trend (categorical data).

\* Statistically significant difference between group 1 compared to groups 2 and 3, <sup>†</sup> Statistically significant difference between group 2 compared to group 1 <sup>§</sup> Statistically significant difference between group 3 compared to groups 1 and 2.

**Table 3:** Multivariate logistic regression analysis for adverse pregnancy outcomes in women with pre-pregnancy chronic hypertension stratified according to blood pressure control at first hospital visit.

Adverse pregnancy outcome	B value	Odds Ratio	95% CI	P value
<b>Severe hypertension</b>				
Hypertensive despite medication (Group 3)	2.22	9.2	5.34 - 15.89	<0.0001
Normotensive with medication (Group 2)	0.93	2.5	1.47 – 4.43	0.001
Normotensive without medication (Group 1)		reference		
<b>Preeclampsia</b>				
Hypertensive despite medication (Group 3)	0.57	1.8	1.06 – 3.13	0.03
Normotensive with medication (Group 2)	0.53	1.7	1.02 – 2.79	0.02
Normotensive without medication (Group 1)		reference		
Black race	0.56	1.7	1.11 – 2.75	0.01
Family history of preeclampsia	0.59	1.8	1.05 – 3.13	0.03
<b>Small for gestational age (&lt;5<sup>th</sup> percentile)</b>				
Hypertensive despite medication (Group 3)	0.74	2.10	1.30 – 3.38	0.002
Normotensive with medication (Group 2)	0.53	1.71	1.08 – 2.70	0.02
Normotensive without medication (Group 1)		reference		
Previous preeclampsia	0.55	1.75	1.20 – 2.54	0.003
Black race	-0.45	0.64	0.43 – 0.94	0.02
Other race	-1.03	0.35	0.13 – 0.99	0.04

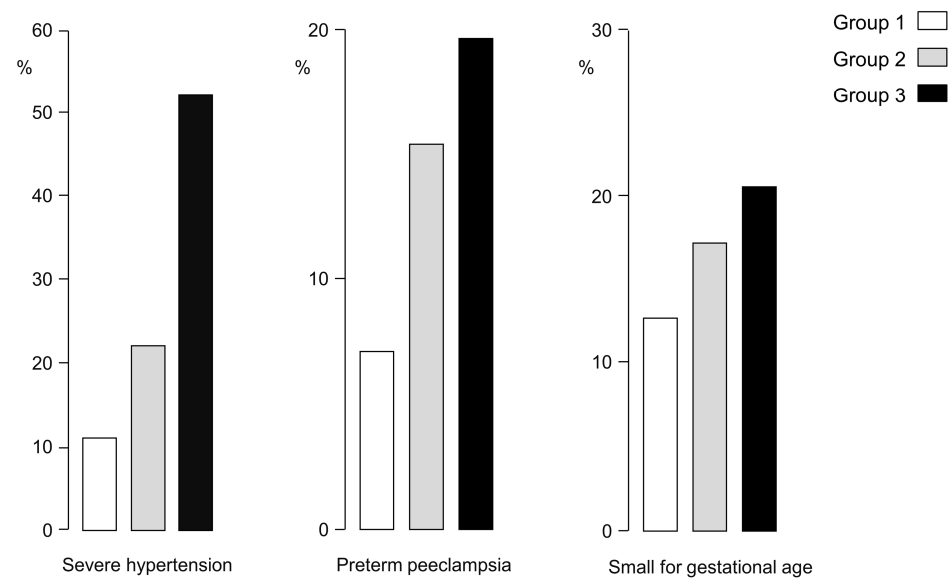


Figure 1.